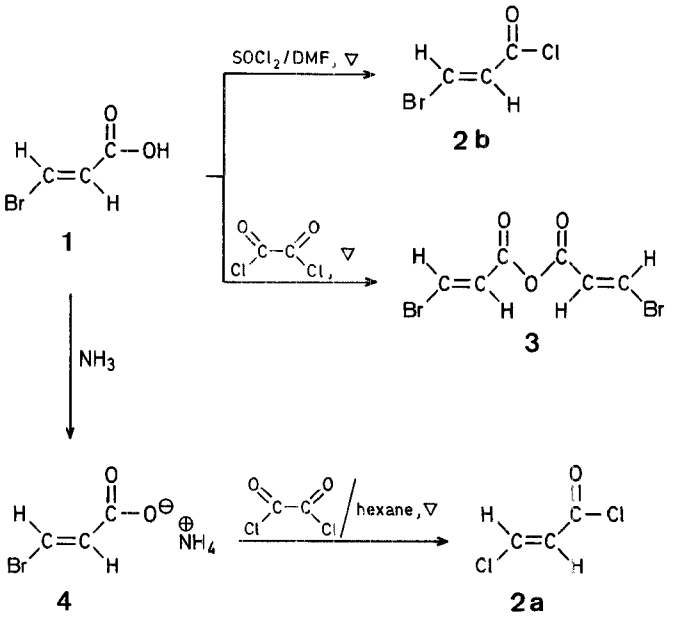
Preparation of β-Haloacryloyl Chlorides

Dennis P. Stack, Robert M. Coates*

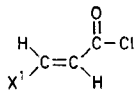
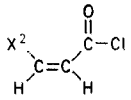
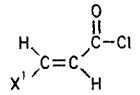
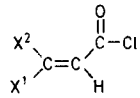
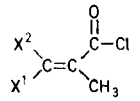
Department of Chemistry, University of Illinois, 1209 W. California Street, Urbana, Illinois 61801, U.S.A.

β-Haloacryloyl chlorides as well as β-haloacrylic esters, amides, and nitriles are useful reagents for Diels-Alder reactions[1,2], Michael additions[3], and conjugate substitution reactions[4,5]. These compounds are commonly prepared from the corresponding β-haloacrylic acids via the acid chlorides[1-8]. In connection with an investigation on Diels-Alder reactions of β-haloacryloyl chlorides, we attempted to prepare the known[7] (*E*)-3-bromoacryloyl chloride (**2b**) from (*E*)-3-bromoacrylic acid (**1**)[7,9] by reaction with thionyl chloride[10], thionyl chloride/catalytic dimethylformamide[11], phosphorus trichloride[4], and benzotrichloride/zinc chloride[7]. However, these reagents either effected simultaneous Cl/Br exchange affording predominantly (*E*)-3-chloroacryloyl chloride (**2a**)[6,7] or gave **2b** in unacceptably low yields. Although (*E*)- and (*Z*)-3-iodoacryloyl chlorides had been obtained with oxalyl chloride[8], (*E*)-3-bromoacrylic acid (**1**) was converted to its anhydride (**3**) by this method. A mild variation of the oxalyl chloride procedure involves the use of the sodium salt[12]. In fact, the reaction of the sodium salt of **1** with oxalyl chloride in hexane afforded **2b** in 51% yield. However, acid chloride **2b** could be more conveniently and efficiently prepared (80%) by reaction of the ammonium salt **4** with oxalyl chloride in refluxing hexane.



The ammonium salt/oxalyl chloride procedure (Method A) provides a mild, general means to prepare a variety of β-haloacryloyl chlorides in good yield and without halide exchange or (*Z*/*E*)-equilibration (Table). Anhydrous ammonium salts are formed in essentially quantitative yield by bubbling ammonia through an ethereal solution of the β-haloacrylic acid. Reaction of the salts with two equivalents of oxalyl chloride in refluxing hexane for 6 h affords β-haloacryloyl chlorides **2a** and **2c–f** in 63–82% yield. This simple two-step procedure should prove useful for the form-

Table. Preparation of β-Haloacryloyl Chlorides (**2**) from β-Haloacrylic Acids

2	Formula	X^1	X^2	Method	Reaction Conditions	Yield[a] [%]	b.p. [°C]/torr	Molecular Formula[b] or b.p. [°C]/torr reported	I.R. (film) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
a		Br		A	reflux, 6 h	80	74–76°/80	38–39°/15[7]	1755; 1595, 1575	6.73 (d, J = 15 Hz, 1 H); 7.92 (d, J = 15 Hz, 1 H)
b		Cl		B	reflux, 1 h	60[c]	114–116°/760	115–116°/760[7]	1767; 1598, 1586	6.53 (d, J = 15 Hz, 1 H); 7.70 (d, J = 15 Hz, 1 H)
c			Br	A	reflux, 6 h	82[d]	65–68°/27–28	56–68°/20[4]	1818, 1763; 1582	6.97 (d, J = 8 Hz, 1 H); 7.18 (d, J = 8 Hz, 1 H)
d			Cl	A	reflux, 6 h	68	63–64°/51–53	99–103°/260[6]	1848, 1766; 1586	6.57 (d, J = 8 Hz, 1 H); 6.87 (d, J = 8 Hz, 1 H)
e		Br		A	reflux, 6 h	72	81–82°/15–16	C_3HBr_2ClO (246.5)	1754; 1598, 1550	8.78 (s, 1 H)
f		Br	Br	A	reflux, 6 h	63	78–81°/11–13	C_3HBr_2ClO (246.5)	1763; 1579	7.37 (s, 1 H)
g		Cl	Cl	B	reflux, 1 h	81	145–147°/760	145°/760[13]	1792, 1768; 1568	6.73 (s, 1 H)
h		Br	H	B	reflux, 1 h	83	59–61°/19	C_4H_4BrClO (183.4)	1746; 1601	2.00 (d, $J \approx 1$ Hz, 3 H); 7.97 (d, $J \approx 1$ Hz, 1 H)
i		H	Br	B	22°C, 16 h	63	68–70°/18–20	C_4H_4BrClO (183.4)	1765; 1603	2.18 (d, J = 1.5 Hz, 3 H); 6.63 (d, J = 1.5 Hz, 1 H)

[a] The purities of the products are estimated to be at least 90–95% based on the ^{1}H-N.M.R. spectra.
[b] The microanalyses were in good agreement with the calculated values: C, ±0.20; H, ±0.08; Br, ±0.28; Cl, ±0.25.
[c] About 5% of the *cis*-isomer is present.
[d] About 5% of the *trans*-isomer is present.

ation of other acid-sensitive acid chlorides. Four additional β-haloacryloyl chlorides (**2b** and **2g, h, i**) were also prepared directly from the β-haloacrylic acid with thionyl chloride/catalytic dimethylformamide in hexane (Method B) at reflux for 1 h (**2b, g, h**) or at room temperature for 22 h (**2i**). The last reaction was carried out at room temperature in order to avoid acid-catalyzed (*Z*/*E*)-isomerization.

β-Haloacrylic Acids:

The required β-haloacrylic acids were all known compounds and were with one exception (see below) prepared by literature methods as follows: (E)-*3-bromoacrylic acid* (**1**, 79%)[7], m.p. 115–116.5°C; (E)-*3-chloroacrylic acid* (63%),[7], m.p. 82–83°C; (Z)-*3-bromoacrylic acid* (54%)[14], m.p. 60–62°C, and (53%)[6], 59–61°C; (Z)-*3-chloroacrylic acid* (74%)[6], m.p. 60–62.5°C; (Z)-*2,3-dibromoacrylic acid* (76%)[15], 85–87.5°C; *3,3-dibromoacrylic acid* (51%)[16], m.p. 84–86°C; (E)-*3-bromomethacrylic acid* (63%)[17], m.p. 58–61°C; (Z)-*3-bromomethacrylic acid* (8.7%)[18], m.p. 61–63°C.

3,3-Dichloroacrylic Acid:

A suspension of silver oxide prepared[19] from silver nitrate (85.7 g, 0.504 mol) and sodium hydroxide (43.2 g, 1.08 mol) in water (400 ml) is vigorously stirred and cooled in an ice bath while 3,3-dichloroacrolein[20] (30.0 g, 0.240 mol; b.p. 82–84°C/11 torr) is added over 15 min. Stirring is continued for an additional 30 min as the reaction mixture is allowed to warm to room temperature. The mixture is filtered with suction and the filter cake is washed with water (500 ml) at 60–70°C. The filtrate is cooled to room temperature and extracted with ether (2 × 200 ml). The ether extract is discarded and the aqueous phase acidified with 12 normal hydrochloric acid and again extracted with ether (2 × 200 ml). This ether extract is washed with saturated sodium chloride solution (100 ml) and dried with calcium chloride. The solvent is evaporated under reduced pressure and the residue recrystallized from hexane to afford nearly colorless crystals; yield: 19.8 g (59%); m.p. 72–76°C (Ref.[13], m.p. 76–77°C).

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 6.40 (s, 1 H, CH–COOH); 12.07 ppm (s, 1 H, COOH).

β-Haloacryloyl Chlorides (2); Typical Procedures:

Method A, via the Ammonium Salt **4**:

(E)-*3-Bromoacryloyl Chloride* (**2a**): Anhydrous ammonia is bubbled into a solution of (*E*)-3-bromoacrylic acid (**1**; 20.3 g, 0.134 mol) in anhydrous ether (200 ml) for 5–10 min to ensure complete reaction. Filtration, washing of the solid on the filter with anhydrous ether (50 ml), and drying at room temperature at 0.1 torr for 2 h gives the colorless, finely divided salt **4**; yield: 22.5 g (100%).

The anhydrous salt **4** (22.5 g, 0.134 mol) is added in 1–2 g portions to a stirred solution of oxalyl chloride (35 g, 24 ml, 0.28 mol) in dry hexane (50 ml) over a 15 min period. The resultant mixture is heated at gentle reflux (oil bath temperature at 80°C) for 6 h, then cooled in an ice bath. The ammonium chloride is filtered off and the precipitate is washed with dry hexane (50 ml). The filtrate is concentrated by distillation at atmospheric pressure through a 15-cm Vigreux column to remove solvent and excess oxalyl chloride. Distillation of the yellow liquid residue under reduced pressure through a 7-cm Vigreux column affords product **2a** as a colorless liquid; yield: 18.2 g (80%); b.p. 74–76°C/80 torr (Ref.[7], b.p. 38–39°C/15 torr).

Acid chlorides **2c–f** are prepared in a similar manner (0.028–0.10 mol scale) and purified by distillation through a 7-cm Vigreux column or 7-cm column packed with glass helices.

Method B, using Thionyl Chloride/Dimethylformamide:

(E)-*3-Chloroacryloyl Chloride* (**2b**): A mixture of (*E*)-3-chloroacrylic acid (9.00 g, 0.084 mol), hexane (20 ml), thionyl chloride (10 ml, 6.0 g, 0.14 mol), and dimethylformamide (5 drops) is heated under reflux for 1 h. The resultant yellow solution is cooled to room temperature and filtered. Concentration of the solution by fractional distillation at atmospheric pressure through a 15-cm Vigreux column followed by distillation of the residue affords **2b** as a colorless liquid; yield: 6.3 g (60%); b.p. 114–116°C/760 torr (Ref.[7], b.p. 115–116°/760 torr).

Acid chlorides **2g** and **2h** are prepared in the same manner (0.091–0.12 mol scale) and purified by distillation through a 7-cm Vigreux column.

(Z)-*2-Methyl-3-bromoacryloyl Chloride* (**2i**): A mixture of (*Z*)-3-bromomethacrylic acid (11.5 g, 69.7 mmol), thionyl chloride (5.5 ml, 9.0 g, 76 mmol), and pentane (10 ml) is stirred at room temperature for 16 h. The solvent and excess thionyl chloride are evaporated under reduced pressure. Vacuum distillation of the yellow liquid residue through a 7-cm Vigreux column affords **2i** as a pale yellow liquid; yield: 8.11 g (63%); b.p. 68–70°C/18–20 torr.

C_4H_4BrClO	calc.	C 26.19	H 2.20	Br 43.56	Cl 19.33
(183.4)	found	26.37	2.19	43.32	19.23

This research was supported in part by grants from the National Science Foundation (Nos. 79-06-05287 and 81-11843).

Received: September 15, 1983

* Address for correspondence.

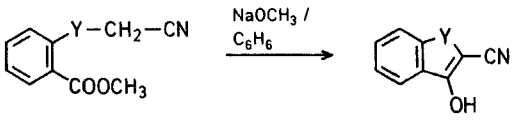
1 E.J. Corey et al., *J. Am. Chem. Soc.* **100**, 8034 (1978).
2 P.K. Freeman, B.K. Stevenson, D.M. Balls, D.H. Jones, *J. Org. Chem.* **39**, 546 (1974).
3 R.K. Boeckman, J.P. Berhas, J. Clardy, B. Solheim, *J. Org. Chem.* **42**, 3630 (1977).
4 J. Dabrowski, K. Kamienska-Trela, L. Kania, *Tetrahedron* **32**, 1025 (1976).
5 J. Alexander, G. Lowe, N.K. McCullum, G.K. Graham, *J. Chem. Soc. Perkin Trans. 1* **1974**, 2092.
6 A.N. Kurtz et al., *J. Org. Chem.* **30**, 3141 (1965).
7 E. Gryskiewicz-Trochimowski, W. Schmidt, O. Gryskiewicz-Trochimowski, *Bull. Soc. Chim. Fr.* **1948**, 593.
8 R.M. Wilson, T.J. Commons, *J. Org. Chem.* **40**, 3891 (1975).
9 H.J. Backer, E.A. Beute, *Recl. Trav. Chim. Pays-Bas* **54**, 167 (1935).
10 D.E. McGreer, B.D. Page, D.P. Kaushal, *Can. J. Chem.* **51**, 1239 (1973).
11 H.H. Bosshard, R. Morg, M. Schmid, H. Zollinger, *Helv. Chim. Acta* **42**, 1653 (1959).
12 A.L. Wilds, C.H. Shunk, *J. Am. Chem. Soc.* **70**, 2427 (1948).
13 O. Wallach, *Liebigs Ann. Chem.* **193**, 1 (1878).
14 C. Rappe, *Acta Chem. Scand.* **19**, 31 (1965).
15 F. Montanari, A. Negrini, *Gazz. Chim. Ital.* **87**, 1102 (1957).
16 C. Rappe, K. Andersson, *Ark. Kemi* **24**, 303 (1965).
17 C. Kolbe, *J. Prakt. Chem.* [2] **25**, 369 (1882).
18 C. Rappe, K. Andersson, *Acta Chem. Scand.* **21**, 1741 (1967).
19 E. Campaigne, W.M. Le Suer, *Org. Synth. Coll. Vol.* IV, 919 (1963).
20 M. Julia, J. Bullot, *Bull. Soc. Chim. Fr.* **1959**, 1823.

Errata and Addenda 1984

M.H. Elnagdi, M.R.H. Elmoghayar, G.E.H. Elgemeie, *Synthesis* **1984** (1), 1–26:

The second paragraph on page 2 should read:
Cyclic 3-oxoalkanenitriles **11** are obtained via cyclisation of methyl *N*-acetyl-*N*-cyanomethylanthranilate (**10a**)[61a], methyl 2-(cyanomethoxy)-benzoate (**10b**)[61b], or methyl 2-(cyanomethylthio)-benzoate (**10c**)[61] under basic conditions.

The formula scheme **10** → **11** (p. 3) should be:



10a Y = N–CO–CH$_3$
b Y = O
c Y = S

11a-c

The experimental procedure for **11a** (p. 3) should read:

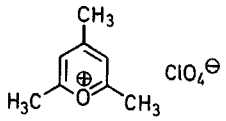
2-Cyano-3-hydroxyindole (11a; Y = NH)[61]:
A mixture of freshly prepared sodium methoxide (10 mmol) and methyl *N*-acetyl-*N*-cyanomethylanthranilate (**10a**; 10 mmol) in benzene (25 ml) is stirred for 2 h at room temperature then left for 12 h at room temperature. The mixture is poured into water. Carbon dioxide is bubbled into the resulting solution till no more solid separates. The product is collected and recrystallised; yield: 64%; m.p. 165–167°C (dec.).

The following references should be added (p. 23):

[61] (a) D. Vorländer, *Ber. Dtsch. Chem. Ges.* **35**, 1683, 1696 (1902).
(b) R. Bryant, D.L. Haslam, *J. Chem. Soc.* **1965**, 2361.

P. Molina, A. Tárraga, E. Romero, M.L. Peña, *Synthesis* **1984** (1), 71–73:

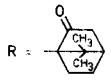
The structure of compound **6** (p. 71) should be:



6

Abstract 6803, *Synthesis* **1984** (1), 82:

The substituent R should be:

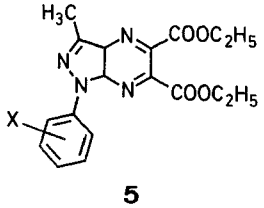


F. Pochat, *Synthesis* **1984** (2), 146–148:

Compounds **3c**, **5c**, and **5g** (p. 147 and 148) should be named as *N'*-acyl-*N'*-(methylthiomethyl)-hydrazones.

P.G. Baraldi, D. Simoni, V. Periotto, S. Manfredini, M. Guarneri, *Synthesis* **1984** (2), 148–149:

The structure of compound **5** (p. 149) should be:



5

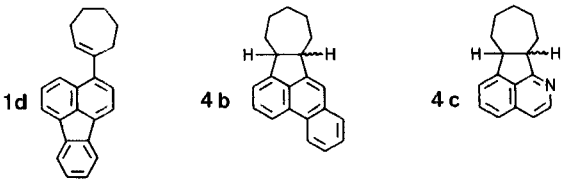
S.C.W. Coltman, S.C. Eyley, R.A. Raphael, *Synthesis* **1984** (2), 150–152:

The first line of the experimental procedure for esters **4** should read:
To a solution of **2** (0.1 mol) in absolute ethanol (30 ml) is added a 1

R. Lapouyade, A. Nourmamode, *Synthesis* **1984** (2), 161–164:

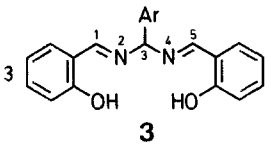
The title should read:
A New Synthesis of 6b,8,9,10,11,11a-Hexahydro-7*H*-cyclohepta[*a*]acenaphthylenes by Base-Catalyzed Photocyclization of 1-Arylcycloheptenes

The structures of products **1d**, **4b**, and **4c** in Tables 2 and 3 (p. 163) should be:



T. Takajo, S. Kambe, W. Ando, *Synthesis* **1984** (3), 256–259:

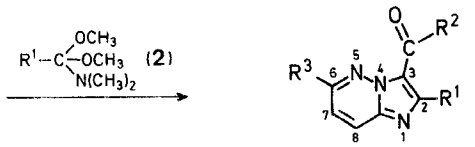
The structure of product **3** (p. 257, left) should be:



3

S. Podergajs, B. Stanovnik, M. Tišler, *Synthesis* **1984** (3), 263–265:

The structures of reagent **2** and products **5a–d** (p. 264) should be:



5a-d

U. Schöllkopf, U. Busse, R. Kilger, P. Lehr, *Synthesis* **1984** (3), 271–274:

The heading for the first experimental procedure (p. 274) should be:
(3*S*,6*S*)-3,6-Diisobutyl-2,5-dioxohexahydropyrazine (**9**):

J. Cabré, A.L. Palomo, *Synthesis* **1984** (5), 413–417:

The authors' address should read:
Gema S.A., Beethoven-15, Barcelona-21; Centro Marga para la Investigación, Muntaner 212, Barcelona-36, Spain
The formulae of Schemes **A** and **B** (p. 413) should be interchanged.
The following experimental procedure should be added:

Cyclohexylammonium Carboxylates (Tables 3); General Procedure:
To a solution of cyclohexylamine (1.15 ml, 10.0 mmol) in the solvent (20 ml, Table 3), the carboxylic acid is added at room temperature. The mixture is stirred for 15 min at room temperature and then cooled to 0–5°C. The precipitate is filtered and washed with cold (0 to −5°C) solvent (10 ml).

D.P. Stack, R.M. Coates, *Synthesis* **1984** (5), 434–436:

The structure of product **2e** (Table, p. 435) should be: